Letters to Editor

A single fatal dose of olanzapine

Sir,
A 52-year male presented with acute onset clouding of consciousness, rigidity, diaphoresis, urinary incontinence, and myoclonic jerks. He had recently developed a stress induced mood disturbance for which he was prescribed olanzapine. He had consumed a single 5 mg dose of the drug on the previous morning. Two hours post admission he developed high rise of temperature with further deterioration of sensorium. Neurological examination revealed a Glasgow coma scale score of 6, 'lead-pipe' rigidity, generalized myoclonus, and brisk deep tendon reflexes. The serum creatinine phosphokinase (CPK) level was 8,240 U/L, (Normal 60-400 U/L) and urine was positive for myoglobin. We diagnosed the case as neuroleptic malignant syndrome, discontinued olanzapine and initiated bromocriptine and clonazepam. His serum iron level was 18 \text{mg/dl}. Serial CPK estimation showed a gradual normalization over the next eight days but there was little improvement in his sensorium even one month after CPK normalization. Prolonged recumbence resulted in multiple pressure sores and he eventually succumbed to aspiration pneumonia eight weeks after his admission.

Neuroleptic malignant syndrome (NMS) is a potentially fatal drug induced movement disorder. Although myoclonus is only occasionally seen,[1] our case had a prominent myoclonic element with severe rigidity. Our patient did meet the criterion for catatonia; however, it differs from the functional lethal catatonia because the latter begins usually with extreme psychotic agitation while NMS usually begins with rigidity as in our case. [2] Hypoferremia present in 96\% of cases is an important marker of this disease.[3] Two syndromes closely resemble NMS, viz. Serotonin syndrome and lethal catatonia. But both of them do not have any temporal relation to neuroleptic therapy, which is a usual requisite for NMS. NMS can develop when a neuroleptic is initiated, reintroduced after a drug free period or with change in dosage or potency of the drug. Two-thirds of the cases develop during the first week of drug initiation; however, there are reports of NMS in patients who have been stable on their drugs for months to years. Although among neuroleptics, haloperidol and fluphenazine are the common culprits, newer atypical antipsychotic drugs are being increasingly reported. They have come into wide clinical use due to their reduced propensity to cause extra pyramidal and tardive syndromes and almost all of them are reported to have caused NMS. Decreased serum iron is known to have a modulatory effect on dopamine receptor sensitivity. There are reports of poor benzodiazepene response in patients having low serum iron, as was the case in our patient.[4] With the recent upsurge in the use of atypical antipsychotics, even by the primary care physicians, this potentially fatal complication should always be borne in mind as it warrants a high index of suspicion for diagnosis and early therapeutic intervention to prevent fatality and long-term morbidity.

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Posterior reversible encephalopathy syndrome in systemic lupus erythematosus

Sir,
Posterior reversible encephalopathy syndrome (PRES) is a rapidly resolving neurological condition characterized by headache, nausea, vomiting, altered mental status, visual disturbances, and seizures.[1] It is associated with a multitude of diverse clinical entities.[1] A case of PRES in a systemic lupus erythematosus (SLE) patient is reported here due to its rarity.

A 22-year-old female, diagnosed with SLE at age 19 after presenting with arthritis and nephritis, a positive antinuclear antibody and elevated double-standed
(ds) DNA, was admitted to the hospital with an acute deep venous thrombosis (DVT). She was treated with Enoxaparine sodium 60 mg bid. During the hospitalization, she had an episode of acute arthralgia accompanied by hypoalbuminemia, acitis and generalized edema and treated with intravenous pulse dose metilprednisolone, one dose cyclophosphamide and furosemide infusion. On 10th day, she experienced generalized tonic-clonic seizure, which was controlled by the administration of intravenous diazepam and subsequent loading dose of phenytoin sodium. Her blood pressure was 155/115 mmHg. She was alert, with normal mental status. She had blurring of vision and bilateral extensor plantar responses without any motor deficit. A noncontrast cranial computed tomography (CT) demonstrated multiple focal areas of hypodensity bilaterally in the basal ganglia, parietal, and occipital lobes. The differential diagnosis at this point included central venous thrombosis (CVT), multiple embolic lesions, vertebrobasilar thromboocclusive disease, or widespread inflammatory disease secondary to lupus involving the central nervous system (CNS). Lumbar puncture demonstrated opening pressure of 180 cm H2O with normal cell counts, protein, and glucose levels. Subsequent magnetic resonance imaging (MRI) of the brain confirmed high signal intensity on axial T2 and fluid-attenuated inversion recovery (FLAIR) weighted images in those regions explained on CT and additionally on both frontal lobes. Diffusion-weighted (DW1) images and apparent diffusion coefficient (ADC) map showed slightly hyperintense lesions, compared to normal gray and white matter, consistent with vasogenic edema [Figure 1]. Cranial magnetic resonance venography was normal. The patient was diagnosed as PRES. The abnormalities of vision improved after 48 hours and resolved within five days. The blood pressure was controlled. Ten days after the insult, repeated MRI demonstrated nearly complete resolution of the previously hyperintense lesions. The size of the lesions in right occipital and frontal regions got smaller but persisted [Figure 2].

Figure 1a: Fast FLAIR weighted coroner MRI show hyperintensity in bilateral posterior parietal, occipital and frontal white matter with some involvement of the overlying cortex and in the bilateral lentiform nuclei and corona radiate

Figure 1b: T2 weighted axial MRI show hyperintensity in bilateral posterior parietal, occipital and frontal white matter with some involvement of the overlying cortex and in the bilateral lentiform nuclei and corona radiate

Figure 1c: DW1 images demonstrated bilateral posterior parietal regions to have slightly hyperintense to normal gray and white matter

Figure 1d: These regions were seen as subtle hyperintens, consistent with increased diffusion and vasogenic edema in ADC image
The abrupt onset of CNS symptoms in SLE patients presents a diagnostic and therapeutic challenge. As reported on a recent review of 323 SLE patients, the most common CNS presentations in descending order of frequency were headache, cerebrovascular disease, mood disorders, cognitive dysfunction, seizures, psychosis, anxiety disorder, and acute confusional state. These symptoms may be either due to direct immune mediated injury of the CNS or secondary events (i.e., related to complication of SLE or its treatment).

PRES is an acute or subacute, progressive reversible neurologic syndrome which can mimic neuropsychiatric SLE presentations. Hence, in SLE patients with acute neurologic symptoms in the setting of hypertension, renal insufficiency and immunosuppressive treatment, PRES should be considered as the cause of CNS abnormalities. A total of 30 cases of PRES in SLE patients have been reported in the literature but the true prevalence is unclear. In recent years, another MR technique, echo-planar DWI findings are useful in distinguishing PRES from neuropsychiatric SLE presentations. Regions with vasogenic edema show marked hyperintensity on ADC and mostly iso or hypointensity on DWI. Although the lesions of our patients challenge with this knowledge, according to Ay et al., an increase in T2 signal within regions of vasogenic edema (T2 shine-through) could cause slight DWI hyperintensity.

In conclusion, PRES should be recognized in patients with SLE presenting with CNS findings. It is extremely important to distinguish this syndrome from other causes, since it is reversible and readily treated by controlling blood pressure, discontinuing the offending immunosuppressive agent or decreasing the dose and controlling of seizure activity.

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